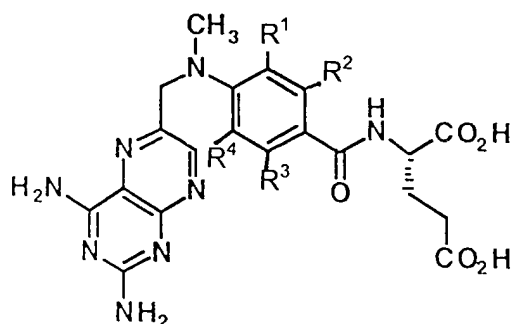


WHAT IS CLAIMED IS:

1. A compound having the structure



wherein R¹-R⁴ are independently fluorine or hydrogen

10 such that at least one of and no more than two of R¹-R⁴ are fluorine.

2. The compound of claim 1, wherein said compound

is *N*-(2-fluoro-4-amino-4-deoxy-*N*-methyl-pteroyl)-*L*-glutamic acid.

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3. A pharmaceutical composition comprising the

compound of claim 1 and a pharmaceutically effective carrier.

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4. A non-invasive method of monitoring tumor tissue concentration of an anticancer drug in real time, comprising:

administering an amount of the compound of claim 1 over a period of time to an individual with the tumor;

5 selecting at least one time point during administration of the compound, after administration of the compound or a combination thereof;

acquiring a magnetic resonance spectrum of an ^{19}F chemical shift of the compound in a volume of the tumor at said
10 time point(s); and

positively correlating a ratio of signal intensities of said ^{19}F shift and an external standard with amount of said compound in the volume of tumor at said time point(s) thereby monitoring the tumor tissue concentration of said compound in real time.

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5. The method of claim 4, further comprising:

positively correlating the tumor tissue concentration of said compound at the time point selected after said period of
20 administration with tumor sensitivity to said compound or with

tumor resistance to said compound, wherein a high concentration of said compound relative to the amount administered correlates with tumor sensitivity or wherein a low concentration of compound relative to the amount administered correlates with tumor resistance; or

comparing the tissue concentration of said compound at the time point selected near the middle of said period of administration with the tumor tissue concentration of said compound at the time point selected after said period of administration, wherein an increase in concentration correlates with tumor sensitivity or a decrease or no increase in concentration correlates with tumor resistance to said compound.

6. The method of claim 5, wherein the time point after said period of administration is at about 0 hours to about 8 hours.

7. The method of claim 5, wherein the time point near the middle of said period of administration is at about 2 hours.

8. The method of claim 5, further comprising:

devising a therapeutic strategy to reduce tumor burden
based on the sensitivity of or resistance of the tumor to said
5 compound; and

reducing tumor burden of said sensitive tumor via
continued administration of said compound; or

reducing tumor burden of said resistant tumors via
administration of a different anticancer compound.

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9. The method of claim 1, wherein said tumor is an
osteosarcoma, a head and neck carcinoma, a bladder carcinoma, a
brain tumor, a lymphoma or a leukemia.

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10. The method of claim 1, wherein said
administration is for a period of time of about 1 hour to about 6
hours.

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11. The method of claim 1, wherein the amount of said
compound administered is about 100 mg/kg body weight to about

1000 mg/kg body weight or about 1 g/m² body surface area to about 12 g/m² body surface area.

12. The method of claim 11, wherein the amount of
5 said compound administered is about 400 mg/kg body weight.

13. A method of non-invasively categorizing a tumor as sensitive or resistant to methotrexate in real time, comprising:
administering an amount of the compound of claim 1
10 over a period of time to an individual with the tumor;
acquiring a magnetic resonance spectrum of an ¹⁹F chemical shift of said compound in a volume of the tumor at a time point selected after the end of said period of administration; and
positively correlating a ratio of signal intensities of said
15 ¹⁹F shift and an external standard with concentration of said compound in the volume of tumor at said time point, wherein a high concentration of said compound relative to the amount administered indicates the tumor is sensitive to said compound or wherein a low concentration of said compound relative to the

amount administered indicates the tumor is resistant to said compound, thereby categorizing said tumor in real time.

14. The method of claim 13, further comprising:

5 devising a therapeutic strategy to reduce tumor burden based on the sensitivity of or resistance of the tumor to said compound; and

 reducing tumor burden of said sensitive tumor via continued administration of said compound; or

10 reducing tumor burden of said resistant tumor via administration of a different anticancer compound.

15 15. The method of claim 13, wherein said administration is for a period of time of about 1 hour to about 6 hours.

 16. The method of claim 13, wherein the time point after said period of administration is at about 0 hours to about 8 hours.

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17. The method of claim 13, wherein said tumor is an osteosarcoma, a head and neck carcinoma, a bladder carcinoma, a brain tumor, a lymphoma or a leukemia.

5 18. The method of claim 13, wherein the amount of said compound administered is about 100 mg/kg body weight to about 1000 mg/kg body weight or about 1 g/m² body surface area to about 12 g/m² body surface area.

10 19. The method of claim 18, wherein the amount of said compound administered is about 400 mg/kg body weight.

20. A method of non-invasively categorizing a tumor as sensitive or resistant to methotrexate in real time, comprising:

15 administering an amount of the compound of claim 1 over a period of time to an individual with the tumor;

 acquiring magnetic resonance spectra of an ¹⁹F chemical shift of said compound in a volume of the tumor at a first time point selected near the middle of said period of administration and at a

second time point selected after the end of said period of administration; and

positively correlating a ratio of signal intensities of said ^{19}F shift and an external standard with concentration of said compound in the volume of tumor at said first and second time points; and

comparing the concentrations of said compound in the tumor volume at said first and second time points, wherein an increase in concentration from said first time point to said second time point indicates said tumor is sensitive to said compound or wherein a decrease or no increase in concentration from said first time point to said second time point indicates said tumor is resistant to said compound, thereby categorizing said tumor in real time.

21. The method of claim 20, further comprising:

devising a therapeutic strategy to reduce tumor burden based on the sensitivity of or resistance of the tumor to said compound; and

reducing tumor burden of said sensitive tumor via continued administration of said compound; or

reducing tumor burden of said resistant tumor via administration of a different anticancer compound.

22. The method of claim 20, wherein said
5 administration is for a period of time of about 1 hour to about 6 hours.

23. The method of claim 20, wherein the time point
after said period of administration is at about 0 hours to about 8
10 hours.

24. The method of claim 20, wherein the time point
near the middle of said period of administration is at about 2 hours.

15 25. The method of claim 20, wherein said tumor is an osteosarcoma, a head and neck carcinoma, a bladder carcinoma, a brain tumor, a lymphoma or a leukemia.

26. The method of claim 20, wherein the amount of
20 said compound administered is about 100 mg/kg body weight to

about 1000 mg/kg body weight or about 1 g/m² body surface area to about 12 g/m² body surface area.

27. The method of claim 26, wherein the amount of
5 said compound administered is about 400 mg/kg body weight.

28. A method of treating a cancer sensitive to methotrexate in an individual, comprising:

administering a therapeutic amount of the compound of
10 claim 1 over a continuous period of time at least once to said individual to reduce tumor burden of said cancer thereby treating said cancer.

29. The method of claim 28, further comprising:
15 acquiring a magnetic resonance spectrum of an ¹⁹F chemical shift of said compound in a volume of the tumor at a time point selected after the end of said period of administration; and

positively correlating a ratio of signal intensities of said
¹⁹F shift and an external standard with concentration of said
20 compound in the volume of tumor at said time point to determine if

the tumor is acquiring resistance to said compound, wherein a high concentration of said compound relative to the amount administered indicates the tumor is not acquiring resistance to said compound.

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30. The method of claim 29, further comprising:

devising an alternate therapeutic strategy if the tumor is acquiring resistance to said compound; and

administering a different anticancer compound to treat

10 said resistant tumor.

31. The method of claim 29, wherein the time point after the end of said period of administration is at about 4 hours to about 8 hours.

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32. The method of claim 28, further comprising:

acquiring magnetic resonance spectra of an ^{19}F chemical shift of said compound in a volume of the tumor at a first time point selected near the middle of said period of administration and at a

second time point selected after the end of said period of administration; and

positively correlating a ratio of signal intensities of said ¹⁹F shift and an external standard with concentration of said compound in the volume of tumor at said first and second time points; and

comparing the concentrations of said compound in the tumor volume at said first and second time points to determine if the tumor is acquiring resistance to said compound, wherein a decrease or no increase in concentration from said first time point to said second time point correlates with acquired tumor resistance to said compound.

33. The method of claim 32, further comprising:

devising an alternate therapeutic strategy if the tumor is acquiring resistant to said compound; and

administering a different anticancer compound to treat said resistant tumor.

34. The method of claim 32, wherein the time point after the end of said period of administration is at about 0 hours to about 8 hours.

5 35. The method of claim 32, wherein the time point near the middle of said period of administration is at about 2 hours.

36. The method of claim 29, wherein said continuous period of time is about 1 hour to about 6 hours.

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37. The method of claim 28, wherein said tumor is an osteosarcoma, a head and neck carcinoma, a bladder tumor, a brain tumor, a lymphoma or a leukemia.

15 38. The method of claim 28, wherein the amount of said compound administered is about 100 mg/kg body weight to about 1000 mg/kg body weight or about 1 g/m² body surface area to about 12 g/m² body surface area.

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39. The method of claim 38, wherein the amount of said compound administered is about 400 mg/kg body weight.